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SUBJECT: Infectious Hepatitis.

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1. Introduction.

a. The detailed clinical and investigative studies of patients ill with infectious hepatitis in MTOUSA during the past 2 years have resulted in the clarification of many features of this disease. Circular Letter No. 37, Office of the Surgeon, NATOUSA, dated 8 July 1944, is hereby rescinded.

b. Infectious hepatitis has been shown to be a disease caused by a virus which has been demonstrated by Paul and others to be in the feces of some patients and is usually present in the blood during the pre-icteric and early icteric stages of the disease. One of the modes of transmission may be water or food contaminated by the infectious agent. Transmission by blood or plasma has been demonstrated. The onset is varied and is usually followed by a clinical course with or without jaundice which may be mild or severe and which usually ends with complete recovery. When recovery does not occur within 4 to 8 weeks, the course of the disease is usually prolonged with a tendency to relapse and chronicity. During the past year in MTOUSA the early recognition of the disease and its subsequent treatment by adequate rest and a diet in which a high protein and low fat content have been emphasized has reduced the group of patients requiring evacuation through medical channels to the Zone of Interior to less than 3 per cent. The ultimate outcome of the disease in such patients is as yet unknown. The secondary attack rate in combat divisions appears to be about 1 per cent. It is possible that there has been a slight increase in the virulence of infectious hepatitis in this theater in that the mortality rate was less than 1 per 1000 during 1943 while it was 3 per 1000 during the year 1944.

2. Nomenclature.

a. The following terms are employed in the classification and disposition of patients with the epidemic form of this disease.

- (1) Hepatitis, infectious, acute, with jaundice.
- (2) Hepatitis, infectious, acute, without jaundice.
- (3) Hepatitis, infectious, chronic, with or without jaundice, (recurrent, relapse and delayed recovery cases).

b. Standard terms indicating other anatomical conditions or diseases of the liver should be used which will separate such diseases from naturally acquired infectious hepatitis.

3. Hepatitis, Infectious, Acute, With Jaundice.

a. The Prodromal Period of 5 - 30 days often presents obscure or bizarre symptoms which at times may make difficult the differential diagnosis between this disease and those of acute enteritis, chronic enteritis, malaria, atypical pneumonia, nasopharyngitis, infectious mononucleosis, brucellosis, sandfly fever, combat exhaustion or psychosomatic states. Although the onset may be insidious, 5 per cent of the patients present high-colored urine followed by icterus as their first and only manifestation during the prodromal period. Ninety per cent of patients "feel sick" with an onset lasting 2 - 5 days which is characterized by:

(1) Chilliness, chills, somnolence and exhaustion.

(2) Fever of 99° spiking to 101 - 104° during first 3 - 4 days without rigors. Occasionally no temperature elevation is recorded.

(3) Anorexia, nausea, and vomiting in 90 per cent, with gripping transient diarrhea or constipation.

(4) Muscular aching of the back near and above the costovertebral angles and extremities which may be severe.

(5) Headache and nuchal resistance which may be severe enough to suggest intracranial disease.

(6) Arthralgia, generalized urticaria, morbilliform rashes or herpes occur in the prodromal period in about 5 per cent of the patients.*

(7) physical findings: A palpable spleen and a palpable tender liver may be found in 15 per cent of the patients at this time or in the interval period. With the patient standing and during forced deep inspiration, abnormal tenderness to finger "dipping" in the epigastrium or right upper quadrant may be elicited. A sharp jolt over the right lower axillary region may cause the patient to flinch with pain and nausea may be induced. Also, if the sitting or stooping patient is grasped from behind under the right costal margin, abnormal pain or tenderness may be found. Enlarged right posterior cervical, right axillary and epitrochlear non-tender, soft glands may be felt. The posterior deep cervical node may be enlarged, soft, freely movable and it is most readily palpated by the rotation of the head to the left and then sliding the fingers gently along the posterior border of the sterno-cleido-mastoid muscle. Although the significance of this sentinel node during early hepatitis is not yet established, it is to be recalled that it makes contact with the lymph channels from the dome of the liver so that it may represent one of the early physical findings of such liver involvement.

(8) Laboratory findings: A normal or leucopenic white count with a relative lymphocytosis is common. The presence of 5 - 40 per cent of immature large vacuolated lymphocytes, averaging commonly about 20 per cent of the white blood cell is of diagnostic significance, when malaria, measles, atypical pneumonia, sandfly fever or infectious mononucleosis can be excluded. Increased bile in the urine, as indicated by increased quantitative urobilinogen and a very strongly positive methylene blue may be found. A positive prompt direct Van den Bergh, bromsulfalein retention of 5 - 20 per cent and a 2+/4+ cephalin-cholesterol

flocculation may be found in the prodromal period. The bromsulfalein test is the single most-helpful test in determining the presence of liver dysfunction during the prodromal stages of hepatitis.

(9) Summary of Prodromal Period. Diagnosis may not be easy in this stage and critical clinical observation and laboratory procedures may be necessary to differentiate hepatitis from malaria, enteritis, atypical pneumonia, infectious mononucleosis, brucellosis, Weill's disease, sandfly fever, upper respiratory infection or other infectious diseases.

b. The Interval period between the prodrome and appearance of jaundice varies between 3 and 14 days in 87 per cent of cases, and in this period the patient may appear to recover from his acute symptoms and request return to duty. The improved condition of the patient and the cessation of the fever has occasionally resulted in the discharge of the patient with a diagnosis of nasopharyngitis, gastro-enteritis or fever of unknown origin. However upon continued observation increasing symptoms may be recorded:

- (1) Anorexia, waves of nausea and vomiting in 50 per cent of patients.
- (2) Ease of fatigue and exhaustion in 95 per cent of the patients.
- (3) Aching or a periodic sticking pain in the right upper quadrant, abdominal distress with fullness, cramps, diarrhea or constipation in 85 per cent of the patients.
- (4) Progressive enlargement of the liver to 3 - 5 centimeters with abnormal tenderness. Examination of the liver should preferably be made at both ends of the day in order that the full effects of activity and rest may be apparent. With the patient standing, tenderness to finger "dipping" in the epigastrium or in the right upper quadrant is marked upon forced inspiration. Abnormal flinch tenderness may be demonstrated by a sharp blow over the right lower axillary region or during deep inspiration with the patient in a stooping or sitting position, and grasped from behind under the right costal margin.
- (5) Either patchy urticaria of the trunk and limbs or a herpes of the upper lip has been observed in 5 per cent of the MTOUSA patients 7 - 10 days before they manifest jaundice. Arthralgia may accompany these early manifestations of the disease.

(6) Dark colored, foamy urine - notably in morning specimens.

(7) Progressive or persistently strongly positive urine bilirubin, methylene blue, or urobilinogen tests. The prompt direct Van den Bergh becomes positive, bromsulfalein retention rises sharply and the cephalin-cholesterol flocculation becomes strongly positive (3+ to 4+) in 92 per cent of the patients. The blood bilirubin or icterus index rises sharply with the onset of icterus.

(8) Summary of Interval Period. The subsidence of the picture simulating an acute infectious disease must not mislead medical officers into the error of discharging the patient to duty when further observation will establish the true diagnosis. Special attention should be paid to the symptoms of abdominal distress, anorexia, nausea, vomiting, continued severe headaches, constipation or cramps and looseness of the bowels. Repeated checks should be made for

changes in size of the spleen and liver together with abnormal tenderness of the latter organ for adenopathy with a falling white count and for a relative lymphocytosis with 10 - 40 per cent of large abnormal lymphocytes. Repeatedly strongly positive methylene blue tests (8 or more drops of 0.25 per cent aqueous sol in 5 cc. urine), or increased urobilinogen tests, rising prompt-direct Van den Bergh reactions and a bromsulfalein retention of 10 - 30 per cent in 45 minutes (5 mgm. per/kilo) may be expected. A strongly positive cephalin-cholesterol flocculation test usually occurs 3 - 7 days before recognizable jaundice in 92 per cent of the cases.

c. The Period of Jaundice. Clinical icterus is observed generally between the 7th - 10th day after the onset of symptoms of the prodromal period and its usual duration is 14 - 21 days. The jaundice varies in degree and in exceptional cases may persist for several weeks or months. The symptoms which appear at the onset of icterus and usually last only 3 - 5 days are:

(1) Anorexia, nausea, vomiting and abdominal cramps.

(2) Right upper quadrant sticking pain or distress, lumbar pain, somnolence, malaise and prostration.

(3) Abdominal pain or headache may be severe.

(4) High backache with local spasm and tenderness of the muscles in the region of the 10th - 12th dorsal and 1st lumbar vertebrae may be a distressing symptom.

(5) The icterus may be mild or severe, short or prolonged, but itching of the skin is uncommon unless urticaria develops. The stools are rarely more than transiently light-colored at the onset of jaundice. At this time the urobilinogen test may be negative.

(6) A transient rise in temperature of 99° or 100° of 1 - 3 days duration may be noted with the appearance of jaundice, following which both the temperature and symptoms rapidly disappear and the patient feels and appears much better except for the deepening icterus.

(7) Physical Examination. The spleen, if enlarged, rapidly becomes normal in size and within a week the enlargement of the liver and tenderness become less marked if the patient remains at bed rest. The soft sentinel lymph nodes of the right deep posterior chain, epitrochlear or axillary nodes which may be enlarged in the interval or pre-icteric period gradually decrease in size so that within 14 - 21 days after the appearance of icterus they may be discernable only as shotty residuals.

(8) The laboratory test of greatest assistance in following the course in this period of the hepatitis is the determination of the icterus index which ranges between 25 - 60 in majority of cases. It usually returns to normal in 14 - 20 days but variations in its titer and duration are to be expected. The quantitative Van den Bergh determination is a most desirable test when facilities for its determination are available. Positive methylene blue reactions parallels the prompt-direct Van den Bergh, thus becoming positive in the pre-icteric stage and persisting through the first 2/3 of the icteric period. The cephalin-cholesterol flocculation is strongly positive from the early icteric stage in

98 per cent of the patients and often parallels the return of the icteric index to normal by becoming negative (0/0) in 14 - 45 days. It is possible that this test reflects parenchymal changes in the liver. The prothrombin shows low normal values except in severe cases in which a falling prothrombin is of grave prognostic significance. The serum proteins are generally elevated due to the fact that the serum globulin fraction is increased from 1 - 4 grams per 100 cc. The bromsulfalein contributes little information in the presence of icterus. The leukocyte count is normal or decreased (8000 - 3500) with a relative lymphocytosis which tends to disappear with the return of the icterus index to normal. The sedimentation rate is slightly slowed in the presence of an elevated blood bilirubin. A sedimentation rate over 20 mm. indicates that a search should be made for the presence of a complication of some disease or infection. If none is found, incomplete recovery from hepatitis should be considered. The serum phosphatase, the hippuric acid and the bilirubin excretion, the glucose and the galactose tolerance tests have not supplied sufficiently helpful information to warrant their general use under conditions which exist in a theater of active operations.

(9) Summary of the Icteric Period. During the icteric stage, the diagnosis is obvious and the strict bed rest, dietary and other special measures should be supported by such laboratory measures which will assist in the evaluation of the severity and prognosis of the case. The icterus index is the most simple test but it is not the most reliable. Experience indicates that the prompt-direct Van den Bergh, the methylene blue and the cephalin-cholesterol flocculation tests may gradually become negative prior to any changes in the patient's jaundice or the icterus index. As soon as the icterus index or the quantitative Van den Bergh tests have returned to normal levels, the bromsulfalein retention test is the most valuable additional guide during the convalescent and reconditioning periods.

d. The period of Convalescence. Convalescence is usually established 20 - 30 days after the onset of infectious hepatitis, although in certain patients convalescence may be markedly retarded. Incomplete bed rest during the acute phases, inadequate food intake, intercurrent infections or surgical procedures have been common factors in delaying recovery. It is during the convalescent stage that the medical officer must employ all of his clinical acumen and essential laboratory aides (bromsulfalein excretion and icterus index or a quantitative bilirubin test) in order to determine when the patient may become ambulatory and subsequently engage in the graduated reconditioning and exercise tolerance test program. The greatest benefit of the esprit de corps of the ward personnel is obtained when officers, nurses, dietitians and enlisted men are motivated with interest in the disease and the knowledge that complete recovery, with return to full activity, is anticipated. Doubt or skepticism as to recovery should not be imparted to those ill with infectious hepatitis. The teamwork of early recognition, adequate complete rest and a special high protein-low fat diet and skillful clinical and nursing direction has resulted in the returning of 95 per cent of all cases of infectious hepatitis to duty. Chronic and delayed recovery cases returned to the Zone of Interior because of a 120-day evacuation policy has been reduced to less than 3 per cent in MTOUSA during 1944 and 1945. The clinical signs of beginning convalescence are:

(1) Arrest of nausea, vomiting and somnolence, followed by a return of the feeling of well being may be expected in 5 - 7 days after icterus makes its appearance.

(2) The abdominal distress, feeling of fullness and cramps decrease and the appetite becomes normal or even voracious.

(3) The alertness, interest in surroundings and the return of strength tax the ward discipline necessary for continued bed rest of these patients.

(4) The liver usually decreases in size and tenderness by the 7th - 14th day. The urine gradually becomes clear, scleral icterus decreases and a weight gain of 1/4 to 1/2 pound per day is expected if the proper diet is available during this period.

(5) Laboratory data.

(a) The icterix index or quantitative Van den Bergh fall to normal except in rare cases in which they remain slightly elevated for weeks. Caution, additional liver function tests and graduated exercise are indicated as further guides to the ultimate disposition of such patients.

(b) The bromsulfalein test has its greatest value in the convalescent stage. If repeated (5 mgm. per/kilogram at 45 minutes) at 5 - 7 day intervals when and after the icterus index has returned to normal, it has been demonstrated that 5 or less per cent of the dye is retained if recovery has been attained. If the bromsulfalein shows a retention of 8 or more per cent at 45 minutes, it is unlikely that the graduated exercise program will be successfully completed. If the test is abnormal, repeated bromsulfalein excretion tests aids clinical judgment regarding spontaneous relapses which may occur even while the patient is still in bed (5th - 6th week of disease). Relapses induced by ward or reconditioning activities are similarly most readily detected and differentiated from functional complaints by the use of this test.

(c) If the cephalin-cholesterol flocculation test has been done, a 1+ or 2+ may persist well into the convalescent and reconditioning periods. However, experience of the past year indicates that it should generally be negative by the 20th - 40th day of the disease if proper treatment has been given the patient. A strongly positive test (4+) in the convalescent period is a caution signal but it must be remembered that the cephalin-cholesterol flocculation test is not specific and it does not differentiate between infectious hepatitis and other diseases causing liver damage, such as amoebic infections, malaria, atypical pneumonia, brucellosis, infectious mononucleosis, Kala-azar and other diseases or agents which damage the parenchyma of the liver or which alter the blood serum proteins. It is chiefly valuable in the interval or pre-icteric stage. If positive the test may indicate continued parenchymal activity during the convalescent period. Studies in progress with the thymol turbidity test (MacLagen) suggest that a much more stable and simply-performed test which may be read in 15 minutes may be available for the evaluation of liver function in hepatitis.

e. Complications of Acute Infectious Hepatitis are:

(1) Acute fulminating diffuse necrosis of the liver with death occurring within 3 - 10 days or less virulent cases in which death occurs within 20 - 30 days and in which some regeneration of liver substance is found.

(2) Chronic, relapsing or delayed recovery cases requiring evacuation to the Zone of Interior occur. The eventual outcome of these patients is unknown.

(3) Low-grade fever (99- 99.5°) of a prolonged and unexplained nature associated with weakness, fatigue and psychosomatic complaints lasting 3 - 4 months. Occasionally these patients have a true relapse.

(4) Intercurrent infections such as nasopharyngitis and pneumonia, because of the demonstrated increased susceptibility of these patients to respiratory infections.

(5) Exacerbation of latent malaria and amoebic colitis.

f. Prognosis of Acute Hepatitis with Jaundice. The course is uneventful in 95 per cent of the cases. In the past year 92 per cent have been returned to full duty within 60 days including the period required for reconditioning and administrative delays. Only 3 per cent have been returned to the Zone of Interior because their recovery was delayed beyond the limitations of the evacuation policy or because of relapses and complications. The final outcome of these patients is unknown.

g. Differential Diagnosis of Hepatitis with Jaundice.

(1) Cholangitis probably cannot be distinguished from infectious hepatitis. However, the leukocytosis, clay colored stools and itching of the skin associated with the elevated cholesterol of the former are points of diagnostic importance.

(2) Leptospiral jaundice has not been a factor in the production of hepatitis in this theater. Conference with local authorities in the Po Valley indicate that the incidence there is high in rice field workers or in people who bathe in the canals or streams that are frequently contaminated by the urine of rats. The severe muscular aching, chills or fever and leukocytosis makes the clinical picture resemble that of many infections and since hepatic and renal involvement are notable in less than half the cases and occur rather late, attention must be given to the history of exposure in an endemic area and a search be made for the organism in the urine and blood if all cases are to be recognized.

(3) Hemolytic jaundice generally presents a long history of repeated recurrences, anemia, reticulocytosis, spherical erythrocytes and increased cell fragility.

poisoning

(4) Carbon tetrachloride is surprisingly common in this theater of operations. Common examples of exposure are:

(a) Riding in a closed cab in which the odor of carbon tetrachloride from a leaking or worn fire extinguisher was unrecognized.

(b) Cleaning clothes in a room without ventilation.

(c) Drinking a small amount by mistake, commonly because it had been put in a canteen or bottle.

(d) Inhalation of fumes from various sources, notably while cleaning of rifles, ordnance of all kinds, etc.

(e) The chief symptoms of carbon tetrachloride poisoning are a sudden onset of nausea, vomiting, headache and prostration followed by jaundice

in 48 - 72 hours. Circumcorneal hemorrhages, nose bleeds, vomiting or passage of blood in the stools or urine are cardinal points. Anuria is present in 1/3 cases and the specific gravity of the urine is low. A sharp elevation of the N.P.N. with little or no increase in the blood urea nitrogen and an elevation of the blood pressure to 150/90 or above are not common in infectious hepatitis but are in carbon tetrachloride poisoning. Severe convulsions may appear suddenly. The recognition of carbon tetrachloride poisoning is important because vigorous infusion of fresh whole blood, plasma, 10% glucose and vitamin K may tide patients over the crisis and then complete recovery follows.

h. Transfusion of Blood and Plasma. Because the infectious agent of hepatitis has been demonstrated in the blood of patients before, during and after the acute stage of the disease, cases resembling the naturally acquired disease should occur. Although statistical evidence is lacking, for patients returned to the Zone of Interior and since the average period of hospitalization of surgical cases is less than 60 days, follow-up studies are needed to demonstrate the full effect of transfusions from the donors who have been long in a heavily infected theater. A recent study of 13,609 battle casualties in MTOUSA showed an attack rate for hepatitis which was low.

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4. Hepatitis, Infectious, Acute, Without Jaundice.

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Hepatitis without jaundice is completely similar to hepatitis with jaundice in so far as prodromal symptoms, physical signs, blood picture, clinical course, prognosis and treatment are concerned except that the height and duration of the elevation of the blood bilirubin are not severe enough to result in clinical icterus. The pathological changes in the livers of patients suffering from hepatitis without jaundice are similar to those with jaundice. The controlled experimental transfer of the disease by Paul, Stokes and others to volunteers in the Zone of Interior has demonstrated that 20 - 40 per cent of the cases may have mild attacks without clinical icterus but with positive laboratory tests. In MTOUSA many initial attacks of hepatitis were mild and the true nature of the disease was not recognized and diagnosis of nasopharyngitis, gastroenteritis, psychosomatic disease or exhaustion were made. This was unfortunate since these patients experienced the same proportion of relapses or complications, and their return to activity before the disease was completely arrested resulted in a recrudescence or recurrence, occasionally associated with jaundice. Such cases were slow to recover. As battalion and other echelon surgeons became experienced with the protean manifestations of hepatitis, fewer diagnostic errors have been made. The experienced medical officer can make the correct diagnosis of hepatitis without jaundice from clinical signs with a fair degree of accuracy. Patients suffering from hepatitis without jaundice should be evaluated, treated and given graduated reconditioning exercises in the same manner as those whose disease is clearly defined by the presence of jaundice.

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a. Incidence of Hepatitis without Jaundice. The actual number of cases of hepatitis without jaundice which may occur in a unit experiencing an epidemic outbreak of this disease is unknown, because it has been impossible in MTOUSA to carry out the continued epidemiological, clinical and laboratory studies which would be necessary for obtaining such information. It appears likely, from epidemiological and experimental studies, that during an epidemic outbreak of the natural disease, many individuals may have mild attacks of hepatitis which are never recognized as such. In a study of homologous serum hepatitis following the use of serum-suspended yellow fever vaccine, it was determined that there

were approximately $2\frac{1}{2}$ cases of hepatitis without jaundice for each one with jaundice, while in a careful study of a natural epidemic outbreak of this disease, roughly $\frac{1}{3}$ of all of the cases of hepatitis were found not to be jaundiced. The incidence of cases without jaundice is low when an outbreak starts but as the epidemic in the unit progresses, the cases appear to become milder and have a shorter duration so that the blood bilirubin does not rise sufficiently or persist long enough to produce jaundice. However, failure to recognize these cases and to keep them in bed under proper therapy has resulted in the occurrence of a larger per cent of chronic or relapsing cases than when they are properly treated.

b. Prognosis of Hepatitis without Jaundice. The course is milder and of shorter duration than when icterus is present - 90 per cent of the cases have been returned to combat duty within 40 days (which include the successful completion of the graduated exercise program). A danger lies in the failure to recognize non-icteric episodes of this disease because the 2nd or 3rd relapse may end fatally.

c. Differential Diagnosis. Hepatitis without jaundice may present one of the most difficult problems in diagnosis, but patients complaining of easy fatigability, exhaustion, right upper quadrant or abdominal distress, cramps, bloating, intolerance for fatty food, continuous headache, backache and depression and in whom an abnormally tender and enlarged liver is felt and whose blood shows a leukopenia, with a relative lymphocytosis and a normal sedimentation rate may well have the disease. The exercise test in such patients is nearly always positive and is associated with an increased bromsulfalein retention and an increase of the prompt-direct van den Bergh.

(1) Gastro-intestinal conditions such as chronic diarrhea, spastic bowel, duodenal ulcer, amoebic colitis, and cholecystitis must be ruled out by the usual methods. It must be remembered that an absent or faint gall bladder shadow may be obtained during and for 6 - 8 weeks after infectious hepatitis.

(2) Psychoneurosis or other psychosomatic conditions may be readily confused with hepatitis without jaundice but the exercise tolerance test and laboratory tests will be negative in such conditions. The psychoneurotic retains his symptoms even after 10 days of absolute rest which helps to exclude hepatitis without jaundice which ordinarily is improved by bed rest.

(3) Atypical pneumonia and malaria are confusing at times but the positive blood smears or x-rays supply an early solution to the differential diagnosis of these diseases. All three tests of methylene blue, bromsulfalein retention and cephalin-cholesterol flocculation are usually strongly and persistently positive in hepatitis which is not true in malaria, pneumonia or other infections in which one of the tests may be positive while the other two are not.

(4) Cirrhosis of the liver has been rare in MFOUSA.

(5) A palpable liver or hepatomegaly may be a normal or incidental finding which may be confused with a diseased liver. A palpable liver was found in 16 per cent of a sample of new men entering MFOUSA directly from the United States and variable degrees of tenderness were noted in 13 per cent of these without supporting clinical or laboratory evidence of hepatitis. No contra-indication for duty has been noted in soldiers with the hepatomegaly which may follow malaria, infectious hepatitis, toxic hepatitis or syphilis of the liver providing they show no increase of symptoms, further enlargement of their liver

and/or aggravation of existing liver function tests when these patients are subjected to vigorous graduated exercises for 5 - 10 days. The early application of this test (see rehabilitation exercise tolerance) will clarify the status of many patients complaining of symptom of alleged or actual latent hepatitis. The following group of clinical problems and their evaluation may be summarized by stating that:

(a) Patients having a palpable, tender liver associated with symptoms of indigestion, fatigue and right upper quadrant distress usually will be shown to have an active hepatitis by the exercise test, and will be indicated by the development of anorexia, nausea, increased liver tenderness, the retention of bromsulfalein and, at times, by an abnormal prompt-direct Van den Bergh and a positive cephalin-cholesterol flocculation test. These patients should be returned to bed for further observation and therapy.

(b) Patients having a large palpable and sharp-edged, non-tender liver without associated symptoms are without clinical importance.

(c) The finding of a palpable or large liver in a patient complaining of vague gastro-intestinal symptoms is not a contraindication for prompt return to his previous duties, if the exercise tolerance and laboratory tests are negative.

(d) Patients with enlarged livers and definitely positive tests of bromsulfalein retention or cephalin-cholesterol flocculation which are unchanged by rest or graduated exercise may be returned to limited assignment duties and should be observed at periods of three months.

(e) Patients with transiently enlarged tender livers with sharp bromsulfalein retention and positive cephalin-cholesterol precipitation occasionally encountered in acute infections such as atypical pneumonia, malaria and enteritis may temporarily simulate latent infectious hepatitis. When the diagnosis is established, no treatment or hospitalization is required in addition to that ordinarily given that particular disease. However, it is wise to repeat these tests during their convalescence, because acute infectious hepatitis may develop during the period of recovery from any disease or injury.

(f) The common problem of the patient with a palpable liver or right upper quadrant tenderness coupled with symptoms of fatigue and indigestion which do not improve sharply after ten days bed rest suggests the need for a psychiatric consultation. Liver function tests in this group of patients are usually normal and are unaltered by the exercise test.

d. Relapsing and Chronic Hepatitis made up 2.9 per cent of a carefully observed series in a General Hospital. Of these relapses, $37\frac{1}{2}$ per cent were sequels to the acute stage and occurred during convalescence while $32\frac{1}{2}$ per cent of the relapses occurred after return to duty, and 25 per cent had had repeated relapses, without showing a tendency to recover and were, therefore, classed as chronic. Spontaneous relapses as indicated by return of lassitude, fatigue, anorexia, gassy indigestion, abdominal distress, diarrhea, tenderness of the liver, sharp increases in the bromsulfalein retention occur surprisingly often at the 4 - 6th week of the disease, often before the patient has been out of bed. Return to absolute bed rest for an additional 2 - 3 weeks if the patient has been ambulatory usually results in recovery but careful observations of such

patients during the reconditioning period should be made. Relapses of hepatitis with or without jaundice are often more severe and more prolonged than the original attack. The chronic cases often give histories of repeated hospitalization, periods of status in quarters and part-time duty while trying to carry on their job. Although the clinical course varies in degree, the symptoms and signs of chronic hepatitis are remarkably constant and once such a diagnosis is established their return to the Zone of Interior is recommended.

5. Treatment of Infectious Hepatitis.

a. The cardinal principles for the reduction in severity and duration of this disease and for the early and safe return of the greatest number of patients to full duty have been found to be its early recognition, real bed rest for the proper length of time, the ingestion of a special nutritious diet and a supervised, graduated reconditioning program. Therefore, the first principle of therapy begins with the medical officer who first must make the decision as to the actual or suspected nature of the soldier's complaint.

(1) Early recognition has been shown to be of great importance because patients recognized as having infectious hepatitis in the pre-icteric stage may never develop an objective jaundice if properly treated. Such patients do not become as ill because they do not have to overcome the effects of a fluid and nutritional debt which aggravates the degree of icterus. Statistics reveal that the degree of icterus reflect roughly the duration of hospitalization which are as follows:

Icterus Index 0 - 30 requires 40 days hospitalization.
Icterus Index 40 - 60 requires 65 days hospitalization.
Icterus Index 75 plus requires 75 or more days hospitalization.

(2) Fluid, Plasma and Blood. If nausea or vomiting are noted on admission of the patient to the field, evacuation or base section hospitals, the following regime has been employed with benefit:

- (a) 1 unit of plasma (250 cc.) each 6 - 8 hours for 2 days (or until nausea and vomiting stop).
- (b) 1 liter of 5 per cent glucose solution (in physiological saline) after each unit of plasma.
- (c) 4 glasses of skim milk solution (50 grams skim milk powder per glass) daily or more if desired.

This procedure results in the early restoration of fluid balance and it supplies most of the basic requirement of ideal protein substance for protection of the liver and for its repair. Nausea and vomiting usually ceases within 12 - 24 hours and is associated with a marked improvement of the depression, somnolence and appetite. The patient is then able to tolerate almost all available foods outlined in the special diet. If plans permit a 2 - 5 day rest on such a diet before the handling and jolting usually experienced during evacuation to base section hospitals, convalescence is usually hastened. Whole fresh blood is recommended in those cases showing hemorrhagic tendencies or in the fulminating types of hepatitis. A routine of 1 pint fresh blood, 1 unit of plasma and 1 liter of 5% glucose and repeated each 8 hours during the crisis is believed by certain observers to be of value. In addition, gamma globulin 50 cc. daily for 3 - 4 days

has been given intramuscularly but its value is not yet established. Vitamin K in ordinary doses has not been effective in this theater. Large doses have not been tried. The symptoms and signs of the disease can be aggravated by dehydration or by excessive fluid administration, especially of intravenous sodium chloride. The administration of the latter may result in the further distension of the liver. Experience indicates that 3500 - 4000 cc. per day are adequate and a urine volume of 1800 cc. per day is desirable. Water by mouth is preferable but 2 - 3 glasses of fruit juice per day are sometimes relished. Beer and other alcoholic beverages are excluded.

(3) Diet. A special high protein - very low fat diet with liberal amount of carbohydrate (200 grams protein, 40-50 grams fat, 400 grams carbohydrate) has been tolerated and relished by patients as soon as the acute stage of nausea and vomiting has passed. The protein has been supplied in 2 full servings of fresh lean (stripped of fat before cooking) broiling or frying beef and 200 grams of powdered skim milk in solution. Fat as in butter and fresh eggs have been served without apparent gastro-intestinal distress which is to be contrasted to the indigestion, bloating, and decreased caloric intake which often develops following the eating of rancid fats which are present in high concentrations in pork, hamburger, luncheon meat and boiled or stewed beef. Fresh green vegetables are desirable, while canned, pulpy, low caloric, vegetables are usually refused. Cereals, bread, navy beans, corn, peas, fresh potatoes and rice supply most of the carbohydrates in the diet. Such a plan results in the ingestion of 2800 to 5000 calories per day with a weight gain of 2-4 pounds per week. The usual loss of weight and strength is therefore corrected and a better physical state established before the patient becomes ambulatory. Patients who fail to eat or to gain weight should be investigated for other disease or for a psychosomatic condition.

(4) Rest. This measure is imperative during the acute and early convalescent periods and it is most beneficial during the first 25 - 30 days of the disease. Best results have been obtained by requiring patients to remain essentially quiet in their bed at all times during the first 3 weeks except for necessary latrine privileges. Complete cooperation of the nurses and ward men is essential if proper rest is to be obtained. This has been materially aided by the proper indoctrination of patients as to the nature of this disease and by the examples of relapses which inevitably occur if bed rest is not faithfully observed.

(5) Other treatment. Morphine and barbiturates are contraindicated in hepatitis. Belladonna or atropine rarely helps the nausea and cramps. Bile salts occasionally have value in the dyspepsia of chronic cases but they are contraindicated in acute hepatitis. Polyvitamines containing vitamin A, 3-daily have been used but their effect is not known.

6. Rehabilitation.

a. Criteria for determining the Ambulatory Period.

(1) At least 3 - 4 weeks of strict bed rest.

(2) Apparent clinical recovery based on a sense of well-being and a weight gain and on the absence of symptoms, especially lassitude, right upper quadrant pain, headache and anorexia.

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(3) Liver normal of size or if palpable, not tender.

(4) Icterix index or blood bilirubin normal for 1 week.

(5) Bromsulfalein retention (5 mg/kg in 45 minutes) 8 per cent or under (normal 2 per cent or less).

(6) If available, caphalin-cholesterol flocculation test should be 2/ or less.

(7) If 1 or more findings are abnormal, another 10 days bed rest are indicated; then the patient's situation should be reviewed.

b. Graduated exercise tolerance test. This should be carried out on all hepatitis patients before their return to general duty or limited assignment.

(1) Purpose: To determine physical fitness for full active duty.

(2) Applicable: To all male convalescent hepatitis patients whose clinical picture and laboratory tests suggest their fitness for discharge from hospital. A modified test should be used for female patients.

(3) Routine for ambulatory convalescent cases.

(a) Five days about the bedside.

(b) Next 5 days at general ward activities, including walks to Red Cross, movies, Post Exchanges, etc.

(c) Ten days supervised exercises.

1st day - 1 mile walk

2nd day - 2 mile hike and light calisthenics for 15 minutes

3rd day - 3 mile hike and 15 minutes of light calisthenics

4th day - 4 mile hike and 15 minutes of calisthenics with double time and side-straddle hop

5th day - same as 4th day

6th day - regular calisthenics for 15 minutes, 4 mile hike and volley ball for 20 minutes

7th day - same as 6th day

8th day - same as 6th day plus 40 minutes volley ball

9th day - same as 8th day

10th day - same as 8th day and continued if status of a patient is in doubt but outcome of the duty status or the return to bed is evident at this point in 90% of patients.

Emphasis should be placed upon periods of double time, side-straddle hop and games which jolt the liver. The best results are obtained if the program is conducted under the supervision of a specially instructed non-commissioned officer. Patients should be examined daily by the ward surgeon for effect of exercise on the liver and appearance of symptoms. Laboratory examination for a possible increase of bromsulfalein retention and elevation of the blood bilirubin should be repeated just before initiating the exercise test program and at 5 - 7 days during the test.

(4) Physical intolerance or induced relapse.

(a) Symptoms and enlargement and tenderness of liver are usually noted by the 5th day if patient has not recovered.

(b) Return or development of symptoms generally appear as follows:

1. Undue fatigue only partially relieved by sleep.
2. Headache, right upper abdominal, costo-vertebral and lumbar distress.
3. Avoidance of previously enjoyed games, patient rests on bed.
4. Lassitude, somnolence and depression.
5. Indigestion, bloating, anorexia, nausea and vomiting.

(c) Laboratory findings usually become abnormal.

1. Bromsulfalein retention usually sharply increased after the 7th day, ranging 20 - 80 per cent at 45 minutes.
2. The blood bilirubin or icterus index rise over control levels.
3. Cephalin-cholesterol flocculation increased to 2+ - 4+. Often these laboratory tests show abnormal trends by 3 - 5 days before patient notes physical weakness or other symptoms.

(5) Results. Unless complete recovery has been attained, a relapse may be induced by exercise, in:

(a) Acute hepatitis, with or without jaundice, in 35 per cent of cases.

(b) Chronic or recurrent hepatitis with or without jaundice in 70 per cent of cases.

(6) Induced relapse cases should be returned to bed rest and diet for a minimum of 2 weeks.

c. Criteria for Combat Duty.

(1) Clinical evidence of physical fitness for duty.

(2) Normal exercise tolerance test.

(3) Liver normal size or if slightly enlarged, not tender after completion of exercise tolerance test.

(4) No increase of bromsulfalein retention, the icterus index or blood bilirubin.

d. Criteria for Temporary Limited Service or other light duty.

(1) Evidence of arrested hepatitis even though a large, non-tender liver or a positive bromsulfalein test is found, but without aggravation of findings, symptoms or blood bilirubin after 10 days of graduated exercise.

e. Criteria for Further Hospitalization.

(1) Abnormal exercise tolerance test.

(2) Aggravation of control bromsulfalein retention and blood bilirubin.

f. Criteria for Zone of Interior. Patients with active hepatitis, with or without jaundice, who will not recover in 120 days, or the presence of the following findings after 2 months of absolute bed rest:

(1) Large tender liver with symptoms.

(2) Abnormal exercise tolerance test.

(3) Elevated blood bilirubin.

(4) Bromsulfalein retention of 10 per cent or more in 45 minutes that is increased by physical activity.

(5) Evacuation to the Zone of Interior is to be seriously considered when there is a history of one or more relapses of hepatitis within 6 months.

7. Hepatitis Diet.

a. The Quartermaster Corps has been most cooperative in supplying all food constituents necessary for the hepatitis diet. Fresh vegetables and fruit when available have been shown to improve the consumption of the full diet. Unpopular foods are not only uneaten but depress the appetite for the important items. Therefore, the close teamwork between the mess officer, dietitian and nurse are necessary to effect the most successful nutritional program. Frequent joint visits by the chief of the medical service, the chief nurse and dietitian to the kitchen during the preparation of the food, to the ward during its serving and observation of the trays on return from the patients will quickly correct or improve any faults and build morale. The following three sample menus indicate the general plan that has proven successful.

<u>Food</u>	<u>Amount</u>	<u>Calories</u>	<u>Proteins</u>	<u>Fat</u>	<u>CHO</u>
<u>Breakfast</u>					
Fresh Orange	150 gms.	75.0	.135	.3	16.8
St. Apricots	100 gms.	292.0	.5.2	.4	66.9
Cereal, ckd.	100 gms.	64.0	2.3	1.2	11.0
Bread	30 gms.	78.0	2.55	.6	15.7
Jam	1 T.	29.0	.05	.03	7.08
Skim Milk Drink	50 gms.	180.0	17.8	.5	26.0
Coffee	1 cup				
		<u>718.0</u>	<u>28.035</u>	<u>3.03</u>	<u>143.48</u>

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<u>Food</u>	<u>Amount</u>	<u>Calories</u>	<u>Protein</u>	<u>Fat</u>	<u>CHO</u>
<u>Dinner</u>					
Broiled Steak	100 gms.	174.0	30.0	6.0	-
FF Tuna Salad	100 gms.	48.5	6.05	2.7	-
FF String Beans	100 gms.	42.0	2.4	.2	7.7
FF Mashed potato	100 gms.	85.0	2.0	.1	19.1
Bread	30 gms.	78.0	2.55	.6	15.7
Jam	1 T.	29.0	.05	.03	7.08
Skim Milk Drink	50 gms.	180.0	17.8	.5	26.0
Peaches	100 gms.	75.0	.4	.1	18.2
2 Eggs		32.2	10.8	12.0	.8
		<u>743.7</u>	<u>72.05</u>	<u>22.23</u>	<u>94.58</u>
<u>Supper</u>					
FF Roast Beef	100 gms.	174.0	30.0	6.0	-
Fresh Potato	100 gms.	85.0	2.0	.1	19.1
FF Hot Beets	100 gms.	53.0	1.5	.1	11.5
Bread	30 gms.	78.0	2.55	.6	15.7
Jam	1 T.	29.0	.05	.03	7.08
Skim Milk Drink	50 gms.	180.0	17.8	.5	26.0
Pears	100 gms.	75.0	.2	.1	18.4
		<u>674.0</u>	<u>54.10</u>	<u>7.4</u>	<u>97.78</u>
Skim milk (for cooking)	90 gms.	323.1	32.0	0.9	46.8
	<u>TOTAL</u>	<u>2566.8</u>	<u>186.185</u>	<u>33.5</u>	<u>382.64</u>

The above diet plan should not be put into effect until the acute stage is passed. The chilled skim milk, however, should be administered to patients as early in the disease as possible. Butter is relished and 2 - 3 squares per day are well tolerated and improve the flavor of less popular foods. Since most patients will take seconds, and an evening meat sandwich and milk are very popular the caloric intake usually exceeds 3500 calories.

b. The powdered skim milk is a most important element of the diet because of its rich supply of methionine, readily assimilable protein, lactose and minerals. Chilled powdered milk solution (50 grams in 200 cc water) is usually the first and often the only substance which the nauseated patient can retain. Its rich content of protein helps tide over the days when an adequate or proper meat intake may not be possible. It has been found that 1/2 pound of powdered skim milk per man per day may be adequate but many hepatitis patients request and will drink twice this amount with apparent proportional benefit. An occasional patient may refuse the powdered skim milk because of life-long habits, but encouragement or flavoring of the drink usually overcomes his objection. The milk solution is best prepared in the estimated volume required for the day with the proportion of 1 pound skim milk powder with water quantity sufficient to make 1 gallon. Thorough stirring, straining and icing makes the milk drink very palatable.

c. broiling and frying beef, 1 1/2 pounds per man per day, divided into 2 servings are adequate after thorough stripping of all fat before cooking when the average regular Quartermaster issue of fresh beef is being used. It should be emphasized that chopped beef, pork, stewing and boiling meat are rich in fat and should not be drawn for cases suffering with hepatitis. An additional meat sandwich and glass of milk with or without flavoring at 2000 - 2100 hours is

advised for the hepatitis patients. The ambulatory hepatitis patients can man the sandwich bar in the ward so that no additional personnel is required. The extra food, the break of a long evening, and the spirit of the sandwich hour is anticipated by all on the ward.

d. Fresh crunchy vegetables and the seasoning of foods for hepatitis cases with spices, onions, green peppers and Worcestershire sauce improves the palatability of the diet.

e. Interval feedings of candy and coca cola are to be avoided until after the evening meal, because candies or soft drinks lessen the appetite. Numerous instances of the undesirable effects of beer have shown that it should be withheld from the hepatitis ward. The beer drinker often bargains for several extra cans from the ill or the teetotaler, with the result that ward discipline breaks down and the drinker's disease becomes aggravated.

f. Popular Foods.

(1) Meat. Rare roast beef, fresh chicken fricasse, stuffed baked chicken, beef stew with fresh potatoes and onions only and Swiss steak are relished. The latter is prepared by browning the steak in a small amount of Mazola oil and then simmering it in a gravy made of skim milk, flour, onions, worcestershire sauce and seasoning. It has been found that patients on the hepatitis diet prefer a repetition of these meats to a diet varied by the addition of canned meats, no matter how temptingly prepared.

(2) Potato, Or potato Substitutes. Fresh potatoes are savored if they are oven-browned, mashed, creamed, fried or served in a salad with hard-cooked egg whites, green peppers, onions and seasoning. The latter is very popular when served as a hot potato salad with a small amount of vegetable oil in place of the customary cream dressing. Dehydrated potatoes, hash-browned with onions and seasoned well rank high among the favorites. When prepared by any other method, they are generally refused. Italian spaghetti, Spanish rice, noodles with beef gravy (preparation similar to par. (1)) and bread dressing make excellent dishes. Bread dressing is relished most when onions and spices only are added, and is refused when raisins are added.

(3) Vegetables. Corn, peas, succotash, stewed tomatoes, savory onions, raw carrot strips, cabbage salad, fresh tomatoes, fresh tomato - onion salad, green pepper - onion salad and pickled raw onions are relished. Savory onions are prepared by covering each onion (medium size) with a Spanish sauce and baking. To pickle raw sliced onions, add a weak vinegar solution and salt and pepper.

(4) Fruit. Canned or fresh fruit salad, fruit pudding and fruit sherbert are well received. Although stewed fruits are thoroughly disliked as such, they are enjoyed if served in a vanilla or rice pudding.

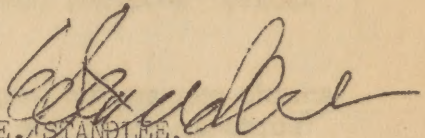
(5) Bread. Plain bread toast, frosted sweet rolls, cinnamon toast and Fresh toast are eaten liberally. A small amount of butter may be used in the preparation of cinnamon toast. A mixture of skim milk, egg white, sugar and salt has proved most satisfactory as a batter in the preparation of French toast. Contrary to expectations, hepatitis patients eat 2 - 4 slices of plain bread per meal, if a jelly spread is available.

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(6) Relishes, condiments, and salad dressings: Catsup, pickled raw onions, mustard sauce, pickle relish, pickles, French dressing, and cream dressing are well liked. French dressing is most palatable to the patient on a hepatitis diet when only a small amount of vegetable oil is used in proportion to the other ingredients. A fat-free dressing can be made of skim milk, vinegar and seasoning. Pickle relish or catsup add variety. Since patients on a hepatitis diet not only enjoy but also tolerate well-seasoned food, it is advisable to use liberal amounts of spices, condiments and relishes to compensate for the lack of flavoring effect of fat in the diet.

(7) Sandwiches served between 2000 and 2100 hours are anticipated and they may be given between meals without impairing the appetite. Steak or roast beef sandwiches are the most popular. Tuna, chicken or salmon salad sandwiches are enjoyed if relishes or condiments are added alone or in combination with a sufficient amount of skim milk to make a creamy spread. An extra glass of milk is generally taken at sandwich time.

For the SURGEON:


E. STANDLEE,
Colonel, M.C.,
Deputy Surgeon.

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